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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,451	02/05/2002	Ronald Brown Miller	222.1101CON	8520

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EXAMINER
CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,451	MILLER ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8,11-16,19-22 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3,6-8,11-16, 19-22 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of response dated 3-24-06 is acknowledged.

Claims 1-3, 6-8, 11-16, 18-22 and 24-25 are pending in the application.

The following rejection of record has been maintained:

1. Claims 1-3, 6-8, 11-16 and 18-22 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 89/09066 (hereafter WO '066).

WO '066 teaches a controlled release composition comprising an active agent, a polymeric matrix comprising a water-soluble polymer and a surface-active agent, for a zero order relelase rate (abstract, page 13, last paragraph; page 14, lines 14-18). The surface-active agents of WO '066 include fatty acid esters and fatty acid ethers having 12 to 24 carbon atoms, which read on the instant hydrophobic fusible agents (page 7, lines 23 to page 8, line 4). WO does not state the melting point, however, instant specification also include fatty acid esters and fatty acid ethers as suitable fusible materials and accordingly, WO '066 meets the claimed requirement. WO '066 teaches polyethylene glycol as a suitable hydrophilic material and recites the molecular weight of PEG that is within the ranged disclosed in the instant specification (page 9, lines 4-17). WO '066 further teaches that the active agent will have a particle size in the range of 0.1 to 500 microns and also disclose multiparticulate forms (page 11; page 17, lines 27-35). With respect to the claimed "extrudate", WO teaches that the composition is extruded (page 18, lines 18-30; page 19, lines 1-5 & lines 12-16 & page 20, lines 8-14). With respect to the claimed water soluble substance, in particular, morphine and the release rates, WO '066 teaches morphine hydrochloride preparation in example of (page 28),

where the composition comprises a matrix formed of a molten mixture of hydrophilic polymer (dextrin) and PEG monostearate was extruded. Thus, WO '066 meets the limitations of claims 6, 13, 19 and 21.

With respect to claim 11, the limitation "the dosage form being obtainable by a process comprising:" even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." With respect to claims 8, 22 and 23, "suitable for once-a-day dosing" is an intended limitation that carries no patentable weight.

WO '066 does not explicitly state the claimed ratios of fusible materials to the polymeric wicking agent, release rates, dissolution parameters i.e., ratio of Cmax to mean plasma levels, tmax, W50 etc., and the claimed test method. However, WO '066 teaches claimed polymers of the matrix and also morphine. WO '066 further teaches that the release of the active agent is achieved for a long time i.e., 8 hours or more (table on page 32). WO '066 teaches that the combination of surface-active agents and the polymer in the matrix enable the release of drug at a substantially constant rate. Therefore, it would have been within the scope of a skilled artisan at the time of the instant invention to optimize the amounts of surface-active agents and the soluble polymer in the formulation of WO '006 such that a homogenous matrix is obtained which provides a zero order release rate of the active agent.

2. Claims 1-3, 6-8, 11-16 and 18-22 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,828,836 to Elger et al (hereafter Elger).

Elger teaches a solid, controlled release pharmaceutical formulation comprising an active agent incorporated in a controlled release matrix comprising a water-soluble polydextrose, for achieving a slow relelase of drug over extended periods of time. (Col. 1). Elger teaches that the matrix also contains at least one digestible C8-C50 substituted or unsubstituted hydrocarbon, especially C12-C36 fatty alcohols, oils, waxes, glyceryl esters of fatty acids etc., and optionally contains hydroxyalkyl or carboxyalkylcellulose (col. 2, lines 11-35). The matrix polymer, polydextrose, and fatty alcohols, waxes, oils etc., taught by Elger read on the instant matrix materials. Although Elger teaches that the melting point of hydrocarbons such as fatty alcohols, waxes etc., ranges from 25 to 90 C (col. 2, lines 23-31). Elger also teaches tablets and capsule, as claimed. The teachings of pellets and granules by Elger meet the claimed particulates because the instant claims do not state the particle size. Elger teaches claimed polymers of the matrix and also teaches various active agents (col. 3) that include the water-soluble active agents such as hydromorphone (col. 3, item 14). Elger further teaches that the release of the active agent is achieved for a long time i.e., 8 hours or more (col. 1, lines 7-12) and figure 2 shows that the release is achieved over 15 -20 hours.

Elger fails to teach exactly the same ratios as claimed, 8:1 to 16:1 and instead teaches a ratio of 1:4 to 4:1. Elger also fails to specify the claimed release rates,

dissolution parameters i.e., ratio of Cmax to mean plasma levels, tmax, W50 etc., and the claimed test method. However, the examples of solid controlled release compositions taught by Elger (in cols. 7 and 8), Elger teaches a higher amount of hydrocarbons as compared to polydextrose. Further, Elger teaches the above matrix components for the same purpose as claimed. Accordingly, optimizing the amounts of the hydrophobic and hydrophilic agents in the compositions of Elger, depending on the drug used i.e., solubility of the drug used and the release type desired so as to achieve a sustained release rate, having the claimed release patterns of a given active agent would have been obvious for one of an ordinary skill in the art. In this regard, instant claims 1 and 11 do not recite any particular drug other than the solubility of the drug. Elger teaches different active agents that are both soluble and insoluble.

The following double patenting rejection of record has been maintained:

Claims 1-3, 6-8, 11-16, 18-22 and 24-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 5,965,163. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant solid, oral, controlled release formulations are generic to the particulate solid dosage forms of the patented claims because instant dependent claim recite microparticulates. Besides, both sets of claims recite the similar matrix and also morphine as the active agent in the dependent claims.

Instant claim 11 recites the product by process claim, which overlaps with the patented product by process claims. The release parameters such as Tmax, Cmax etc., claimed in the patent overlap with the claimed parameters. Accordingly, optimizing the amounts or ratios of the wicking agents and fusible materials responsible for the release of the active agent depending on the desired release rate would have been obvious from the patented claims.

Examiner notes that in response dated 8-16-04, applicants stated that a terminal disclaimer was enclosed in response to the double patenting rejection over US 6,399,096. However, a careful review of the papers submitted with the response of 8-16-04 does not show any terminal disclaimer. Accordingly, the double patenting rejection made previously over US 6,399,096 has been reinstated as follows:

Claims 1-3, 6-8, 11-16, 18-22 and 24-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 11-22 of U.S. Patent No. 6,399,096. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant solid, oral, controlled relelase formulations are generic to all water-soluble active ingredients, including the specific drugs such as morphine, tramadol etc., of the patented claims. Besides, both sets of claims recite that the drug is dispersed in a matrix, which results in the same in vitro dissolution rates. Accordingly, the species of the patented claims anticipates the claimed genus of the instant application, and therefore, a patent to the

genus would necessarily, extend the rights of the species should the genus issue as a patent after the species.

Response to Arguments

Applicant's arguments filed 3-24-06 have been fully considered but they are not persuasive.

WO 89/09066 (WO):

Applicants argue that WO reference fails to teach the claimed ratios of the fusible material and the wicking agent and that the reference teaches away from the claimed high amounts of surface-active agent because WO states that above 50% by weight of surface-active agent, there is a phase inversion and may become a continuous phase. Applicants argue that in contrast to the claimed hydrophobic fusible material to hydrophilic, organic polymeric wicking agent (8:1 to 16:1), '066 describes that the surface active agent is typically present in the composition in an amount of about 2-50% when the active substance does not possess properties of a surface active agent and the surface active agent content of less than 2% may be employed when the active substance possesses surface active agent properties. Therefore, it is argued that one of an ordinary skill in the art would not be motivated to formulate a dosage form having a ratio as claimed. However, the arguments are not persuasive because WO also states that the specific release of an active agent depends upon the active as well as the matrix components. Further, WO also states that the active agent itself can have the surfactant properties. Therefore, optimizing the amounts of the release controlling

surfactants and polymers, so as to achieve the desired release rate, depending on the active agent used in the composition would have been obvious from the teachings of WO '066. While applicants argue that examiner uses hindsight regarding the pharmacokinetic parameters, applicants themselves admit that these parameters vary depending on the numerous factors such as type, amounts active agents and excipients used in the formulation. Instant claims fail to recite any active agent. Further, in the absence of any unexpected results with respect to the claimed ratio of matrix materials, it would have been obvious for one of an ordinary skill in the art to optimize the amounts of the release materials in a dosage form, such that a desired release profile is achieved.

Rejection over Elger et al (US 4,828,836):

Applicants argue that Elger reference fails to teach the claimed ratios of the fusible material and the wicking agent. Applicants state that the polyethylene glycol of Elger is not a hydrophobic and instead a hydrophilic compound, as supported by Annunziata et al. However, while it is agreed that PEG of Elger is hydrophilic, the reference not only teaches PEG but also teach other compounds such as waxes, oils, fatty alcohols, glyceryl esters of fatty acids etc., which have a melting point of 25 to 90 C (col. 2, lines 23-32). Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use a combination of polydextrose and the claimed hydrophobic materials from the teachings of Elger, with an expectation to a sustained release rate of an active agent. Elger teaches all the structural limitation of

the instant composition that has been claimed. Therefore, optimizing the amounts of the release controlling surfactants and polymers, so as to achieve the desired release rate, depending on the active agent used in the composition would have been obvious from the teachings of Elger.

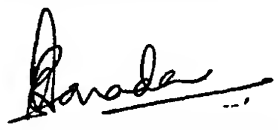
Double patenting rejection: Applicants' arguments regarding the double patenting rejection over US 5,965,163 are not persuasive because the patent claims recite the instant the claimed fusible material, wicking agent, the soluble drug and the particulate forms of the composition. The release parameters such as Tmax, Cmax etc., claimed in the patent overlap with the claimed parameters. Accordingly, optimizing the amounts or ratios of the wicking agents and fusible materials responsible for the release of the active agent depending on the desired release rate would have been obvious from the patented claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -6.30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lakshmi S Channavajjala
Examiner
Art Unit 1615
June 09, 2006